

# PATENT SPECIFICATION

NO DRAWINGS

887,413



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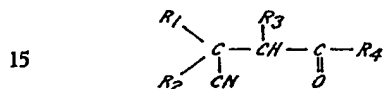
## COMPLETE SPECIFICATION

### Carbocyclic Cyanoketones

We, ROHM & HAAS COMPANY, a corporation organized under the laws of the State of Delaware, United States of America, of 222 West Washington Square, Philadelphia 5, Pennsylvania, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention is concerned with new  $\beta,\beta$ -disubstituted- $\beta$ -cyanoketones.

In brief, this invention provides  $\beta,\beta$ -disubstituted -  $\beta$  - cyanoketones of the formula:

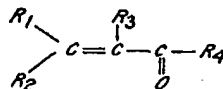


in which  $R_1$ ,  $R_2$ , and  $R_3$  individually represent alkyl, aryl, arylalkyl, or alkylaryl groups and  $R_4$  is a hydrogen atom or a methyl or ethyl group. Alternatively,  $R_1$  and  $R_2$  may be joined together to form a 5- or 6-membered carbocyclic ring with the carbon atoms  $\beta$  to the carbonyl group;  $R_1$  and  $R_3$  may be joined together to form a 5- or 6-membered carbocyclic ring with the carbon atoms  $\alpha$  and  $\beta$  to the carbonyl group;  $R_2$  and  $R_4$  may be joined together to form a 5- or 6-membered carbocyclic ring with the carbonyl atom and the carbon atoms  $\alpha$  and  $\beta$  thereto; and  $R_1$  and  $R_4$  may be joined together to form a 5- or 6-membered carbocyclic ring with the carbonyl atom and the carbon atom  $\alpha$  thereto. In any event, at least one carbocyclic ring is present by virtue of the joinder of a pair of R groups. The total carbon content of the product should preferably not exceed 24 atoms, including the cyano carbon atom.

Preferred sub-classes of compounds are those containing not more than 24 carbon atoms and in which the various R substituents

are as follows: (1)  $R_1$  and  $R_2$  are joined together and (a)  $R_1$  is hydrogen or methyl and  $R_2$  is alkyl or (b)  $R_1$  is hydrogen and  $R_2$  is aralkyl; (2)  $R_2$  and  $R_4$  are joined together and (a)  $R_2$  is alkyl and  $R_4$  is hydrogen or methyl or (b)  $R_2$  is aryl and  $R_4$  is hydrogen; (3)  $R_1$  and  $R_3$  are joined together and (a)  $R_1$  is alkyl and  $R_3$  is aralkyl or (b)  $R_1$  is aralkyl and  $R_3$  is alkyl; (4)  $R_3$  and  $R_4$  are joined together,  $R_1$  is alkyl and  $R_2$  is alkyl, aralkyl or aralkyl; (5)  $R_1$  is joined to  $R_2$  and  $R_3$  is joined to  $R_4$ ; and (6)  $R_1$  is joined to  $R_3$  and  $R_2$  is joined to  $R_4$ .

The compounds of the invention are prepared by the hydrocyanation of an unsaturated ketone of the formula:



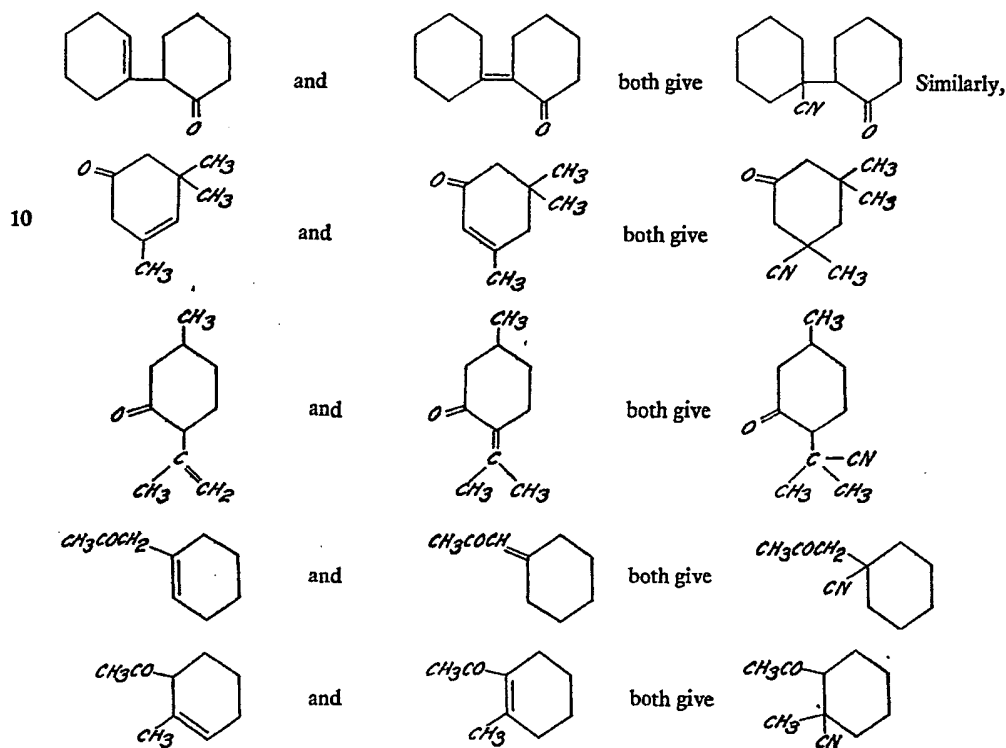
in which  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  are as above defined.

The hydrocyanation reaction is carried out by bringing together hydrocyanic acid and the unsaturated ketone at a temperature in the range from about 125° to 275° C. and in the presence of an alkaline catalyst capable of generating cyanide ion. Also, the hydrocyanic acid is gradually brought into contact with the unsaturated ketone at a rate which is substantially that at which it reacts with the ketone.

The  $\alpha,\beta$ -unsaturated ketone reactant represented by the above formula is frequently present in the form of a mixture with the corresponding  $\beta,\gamma$ -unsaturated ketone tautomer(s) and such tautomeric mixture may be generated under the reaction conditions employed in the preparative method of the invention, it being well known that  $\alpha,\beta$ -unsaturated ketones and  $\beta,\gamma$  unsaturated ketones are in tautomeric equilibrium in the presence of basic compounds. It follows, of course, that  $\beta,\gamma$ -

unsaturated ketones themselves can be used as precursors of the  $\alpha,\beta$  unsaturated compounds since the latter will be formed in the presence of the basic catalyst. Thus for ex-

ample, the  $\beta,\gamma$ -unsaturated ketone, 2-(1-cyclohexenyl) cyclohexanone, is just as satisfactory for the present purpose as the corresponding 2-cyclohexylidenecyclohexanone, i.e.



Typical of the carbocyclic olefinic ketone reactants that may be used are:

- 15 2 - methylcyclopenten - 1 - yl methyl ketone;  
 2 - ethylcyclohexen - 1 - yl benzyl ketone;  
 2 - butylcyclohexen - 1 - yl phenyl ketone;  
 2 - propylcyclopenten - 1 - yl octyl ketone;  
 20 2 - methyl - 3 - butylcyclopenten - 2 - one - 1;  
 2 - ethyl - 3 - octylcyclohexen - 2 - one - 1;  
 2 - methyl - 3 - dodecylcyclohexen - 2 - one - 1;  
 25 3 - hexylcyclopenten - 2 - one - 1;  
 3,5,5 - trimethylcyclohexen - 2 - one - 1;  
 2 - isopropylidene - 5 - methylcyclohexanone;  
 2 - isopropylidene - 6 - methylcyclohexanone;  
 4 - (2 - oxocyclohexylidene)octane;  
 30 2 - cyclohexylidenecyclohexanone;  
 1 - cyclohexylidene - 2 - octanone;  
 2 - cyclopentylidene - 3 - hexanone;  
 6 - cyclopentylidene - 7 - tridecanone;  
 1 - cyclohexylidene - 2 - butanone;  
 35 2 - cyclohexylidenecyclopentanone;  
 2 - cyclopentylidenecyclohexanone; and  
 2 - hexylcyclopenten - 1 - yl butyl ketone.

As indicated, the hydrocyanation reaction is

conducted at a temperature in the range of about 125° to 275° C, this is because temperatures outside this range either result in inappreciable or undesirable results. The preferred temperature range is from 150 to 225° C.

Atmospheric pressure is advantageously employed. Superatmospheric pressures may be employed, if desired, but apparently no appreciable advantages are achieved thereby. If superatmospheric pressures are contemplated, they may be achieved autogenously or with the aid of nitrogen or other inert gas.

The present reaction is preferably conducted on a batch basis but a continuous adaptation may be employed, if desired.

A volatile inert highly polar organic solvent may be employed, if desired. The use of a solvent is especially desirable when the higher-boiling ketone reactants are used. It is frequently desirable to employ a portion of the specific  $\beta,\beta$  - disubstituted -  $\beta$  - cyano-ketone product concerned in the present method as a solvent. Suitable solvents include dimethylformamide, dimethylacetamide, 1-

methyl - 2 - pyrrolidinone, 1,5 - dimethyl-2 - pyrrolidinone and 1,3 - dimethyl - 2-imidazolidinone.

5 An alkaline catalyst capable of generating cyanide ions is required and is preferably used in amounts of about 0.1 to 20% by weight of the total weight of the reactants, is required. Suitable in this respect are alkyl  
10 metals and their carbonates; alkali and alkaline earth metals and their alkoxides, oxides, hydroxides, peroxides, and cyanides; *tert*-amines; and quaternary ammonium bases. Actually, there may be employed as catalyst  
15 any base which has an ionization constant above about  $10^{-7}$  when determined in an aqueous medium. Typical examples of the catalysts that may be used include sodium, potassium, lithium, sodium methoxide, potassium  
20 butoxide, lithium ethoxide, magnesium ethoxide, sodium oxide, potassium hydroxide, calcium oxide, barium hydroxide, strontium hydroxide, sodium peroxide, magnesium  
25 peroxide, potassium cyanide, lithium cyanide, barium cyanide, magnesium cyanide, sodium carbonate, potassium carbonate, trimethylamine, triethylamine, triethanolamine, octyldimethylamine, N-methylmorpholine, benzyltrimethylammonium  
30 hydroxide, dibenzyltrimethylammonium hydroxide and dodecyltriethylammonium hydroxide. The alkali metal cyanides are particularly effective for the instant purposes.

A preferred feature of the process involves bringing together, at the specified reaction temperature, preformed mixtures of (a) the alkaline catalyst and the unsaturated ketone reactant or the desired cyanoketone product and  
35 (b) hydrocyanic acid and the unsaturated ketone reactant.

40 By employing the most preferred reaction conditions described, yields of about 50% to 90% and above can be consistently achieved. Under these preferred reaction conditions, there is substantially no polymerization of the  
45 hydrocyanic acid and there are substantially no cyclization, condensation, or decomposition compounds formed, either or both of which undesired results frequently plague the hydrocyanation procedures known to the art.

50 In a practical way of carrying out the process, whether the continuous or batch embodiment is used, the catalyst and a portion of the ketone reactant is initially charged to the reaction vessel and to this mixture there  
55 is then added a mixture of the same ketone reactant and hydrocyanic acid. Alternatively, it is possible to use as an initial charge to the reaction vessel a mixture of catalyst with a portion of the ketone nitrile product from a  
60 previous run, to this mixture being added a mixture of hydrocyanic acid and ketone reactant. By employing, as part of the initial charge, the ketone reactant or the ketone nitrile product, the formation of undesired  
65 condensation products is reduced to a mini-

mum or entirely eliminated. This leads to maximum yields with minimum amounts of undesired products, which minimizes or substantially eliminates problems of separation and isolation of the product. It is also satisfactory in the present invention, when either a batch or continuous embodiment is used, to add all of the catalyst at the beginning of the reaction or intermittently, as desired. It  
70 should, however, be particularly noted that the hydrocyanic acid should not be added all at once but should be gradually brought into contact with the catalyst mixture at a rate which is substantially that at which it reacts with the ketone. With large amounts of hydrocyanic  
75 acid present at any one time, undesired polymerizations tend to be favoured.

It is possible, in carrying out the reaction, to introduce the hydrocyanic acid into the reaction zone in the gaseous state.  
80

In some cases, it may be that the catalyst is not soluble or at least not entirely soluble in the reaction system, and it is, therefore, desirable to employ agitation such as stirring or rocking or the like in order to insure the highest activity from the catalyst. Agitation of the reaction system is generally advantageous.  
85

At the conclusion of the reaction, the catalyst may be neutralized by the addition of acid, preferably of a mineral acid such as phosphoric, sulfuric or hydrochloric. The reaction mixture may then be filtered, if desired, and then distilled, preferably at reduced pressures. These products are useful as mosquito and rodent repellents when applied in commercial amounts in an inert carrier. They are also valuable as plasticizers for nitrocellulose.  
90

The present invention may be more fully understood from the following examples, which are offered by way of illustration and not by way of limitation. Parts by weight are used throughout.  
95

#### EXAMPLE 1.

100 Into a three-necked flask equipped with a stirrer, thermometer, ice-water cooled condenser and equalized-pressure dropping funnel there are added 293.7 parts of a mixture of 93% 2 - cyclohexen - 1 - yl cyclohexanone and 7% 2 - cyclohexylidenecyclohexanone, 293.7 parts of dimethylformamide, and 5.4 parts of potassium cyanide. The mixture is heated at reflux (160° C.) and a mixture of 46.8 parts of dimethylformamide and 46.8 parts of hydrogen cyanide is added dropwise over a forty-five minute period. During this addition, the temperature drops to 146° C. Stirring and heating are continued for one hour, during which time the temperature rises to 157° C. The reaction mixture is cooled to room temperature and 6.4 parts of aqueous 85% phosphoric acid is added. The mixture is distilled under reduced pressure. The product is collected at 163° to 174° C. at 2.8  
105  
110  
115  
120  
125  
130

mm. absolute pressure. It crystallizes on standing and is recrystallized from boiling isooctane. The recrystallized product is a white solid, melting at 85° to 86° C. and containing 6.80% nitrogen (6.83% theoretical). The product is identified as 1-(2-oxocyclohexyl)cyclohexanecarbonitrile and corresponds to the formula

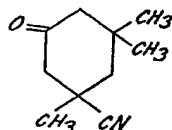


- 10 In a similar manner, there is prepared acetonilcyclohexanecarbonitrile by using as the olefinic carbocyclic ketone reactant an equilibrium mixture of cyclohexen-1-ylacetone and cyclohexylideneacetone. Likewise, 1-cyclohexylidene-2-octanone gives 1-(2-oxooctyl)cyclohexanecarbonitrile and 2-cyclopentylidene-3-hexanone gives 1-(1-methyl-2-oxopentyl)cyclopentanecarbonitrile.

#### EXAMPLE 2.

- 20 Isophorone (552 parts), dimethylacetamide (552 parts), and potassium carbonate (14 parts) are charged to a reactor and heated to 175° C. Liquid hydrogen cyanide (113 parts) is added dropwise during three hours at a rate such that no time does the pot temperature drop below 160° C. Phosphoric acid (23 parts of aqueous 85% strength) is added and the mixture is distilled under reduced pressure. The product (465 parts) has a boiling point of 119° C. at 1.7 mm. absolute pressure and crystallizes on cooling. The product is dissolved in hot isopropanol (1000 parts) and the mixture is then cooled first to 0° then to -25° C. The precipitate which forms is separated by filtration, washed with cold isopropanol, and dried in air at room temperature. The white crystalline product (432 parts) has a melting point of 68° to 70° C. and a nitrogen content of 8.46% (8.48% theoretical).

The product is identified as 5-oxo-1,3,3-trimethylcyclohexanecarbonitrile and corresponds to the formula

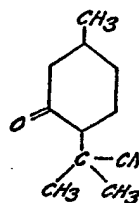


- 45 In like manner, 2-methyl-1-cyclopentenyl methyl ketone gives 2-acetyl-1-methylcyclopentanecarbonitrile, 2-methyl-3-butylcyclopent-2-en-1-one gives 3-oxo-2-methyl-1-butylcyclopentanecarbonitrile, and 2-(1-cyclohexen-1-yl)cyclopentanone

gives 1-(2-oxocyclopentyl)cyclohexanecarbonitrile.

#### EXAMPLE 3.

A mixture of 2-isopropylidene-5-methylcyclohexanone (pulegone) (76 parts), 1-methyl-2-pyrrolidinone (38 parts), and potassium cyanide (1.6 parts) is heated to 180° C. and HCN (14 parts) is added gradually at such a rate that the temperature of the pot never falls below 170° C. The mixture is distilled under reduced pressure to give 81 parts of crude product having a boiling point of 120° to 145° C. at 1.4 mm. absolute pressure. Redistillation under reduced pressure gives the pure liquid product having a boiling point of 120° to 125° C. at 1.4 mm. absolute pressure, an  $n_D^{25}$  value of 1.4669, and a nitrogen content of 7.85% (7.83% theoretical for  $C_{11}H_{17}ON$ ). The product is of the formula:



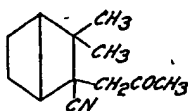
In an entirely similar fashion are prepared 1-(1-pentyl-2-oxooctyl)cyclopentanecarbonitrile from 6-cyclopentylidene-7-oxotridecane, and 1-lauryl-2-methyl-3-oxocyclohexanecarbonitrile from 2-methyl-3-laurylcyclohex-2-en-1-one.

#### EXAMPLE 4.

A mixture of cyclohexylideneacetone (138 parts) and potassium cyanide (3.3 parts) is heated to 150° C. and HCN (30 parts) is added dropwise while the temperature is maintained at 140° to 150° C. When the addition is complete, the mixture is held at 150° to 160° C. for twenty minutes, then is treated with four parts of aqueous 85% phosphoric acid, then distilled under reduced pressure. The product, 1-(2-oxopropyl)cyclohexanecarbonitrile, is obtained in 75% yield and is shown to have the formula  $C_9H_{15}O$  by analysis. The process may be modified by charging 1-(2-oxopropyl)cyclohexanecarbonitrile (20 parts) and potassium cyanide (3.3 parts) to the reactor. This mixture is heated to 150° C. and a mixture of cyclohexylideneacetone (138 parts) and HCN (30 parts) is added slowly while maintaining a temperature of 150° to 160° C. The yield is only 70% in this modification. Temperatures as high as about 200° C. may be employed in this modification with satisfactory yield.

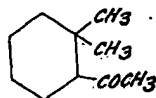
In the same manner, (2,2-dimethylbicyclo[2.2.1]heptanylidene)acetone is converted to 3,3-dimethyl-2-(2-oxopropyl)bicyclo[2.2.1]heptane-2-carbonitrile in 50%

yield; a somewhat better yield being obtained if 1-methyl-2-pyrrolidinone is employed as a solvent. This compound corresponds to the formula:



#### EXAMPLE 5.

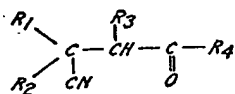
To a mixture of 1-acetyl-2-methylcyclohexene (150 parts), dimethylformamide (50 parts), and sodium cyanide (25 parts) under reflux, is slowly added HCN (30 parts) dissolved in dimethylformamide (50 parts). The temperature is maintained at 145° to 155° C. by regulating the rate of addition of the HCN solution to the reaction mixture. The mixture is heated for one hour after the addition of the acid is completed; then aqueous 85% phosphoric acid (4 parts) is added and the mixture is distilled under reduced pressure. The product is shown to be 2-acetyl-1-methylcyclohexanecarbonitrile by elemental analysis and corresponds to the formula:



Similarly, 2-benzoyl-1-methylcyclopentanecarbonitrile is obtained from 1-benzoyl-2-methylcyclopentene - 1 and 2-stearoyl-1-methylcyclohexanecarbonitrile is obtained from 1-stearoyl-2-methylcyclohexene - 1. A better yield of 2-stearoyl-1-methylcyclohexanecarbonitrile is obtained when 1-methyl-2-pyrrolidinone is employed as solvent instead of dimethylformamide and, if the reaction temperature is raised to 200° to 225° C., an even better yield is obtained. In conclusion, by reason of Section 9 of the Patents Act 1949, reference is directed to U.K. Patent No. 730,209.

#### WHAT WE CLAIM IS:—

1. A  $\beta,\beta$ -disubstituted  $\alpha\beta$ -cyanoketone of the formula:



in which  $R_1$ ,  $R_2$  and  $R_3$ , when not forming part of a cyclic group, each represent an alkyl, aryl, arylalkyl, or alkylaryl group;  $R_3$ , when not forming part of a cyclic group, represents a hydrogen atom, a methyl or ethyl group;  $R_1$

and  $R_2$ , when forming part of a cyclic group, collectively represent a 5- or 6-membered carbocyclic ring together with the carbon atom  $\beta$  to the carbonyl carbon atom;  $R_1$  and  $R_2$ , when forming part of a cyclic group, collectively represent a 5- or 6-membered carbocyclic ring together with the carbon atoms  $\alpha$  and  $\beta$  to the carbonyl carbon atom;  $R_2$  and  $R_3$ , when forming part of a cyclic group, collectively represent a 5- or 6-membered carbocyclic ring together with the carbonyl carbon atom and the carbon atoms  $\alpha$  and  $\beta$  thereto; and  $R_3$  and  $R_4$ , when forming part of a cyclic group, collectively represent a 5- or 6-membered carbocyclic ring together with the carbonyl carbon atom and the carbon atom  $\alpha$  thereto, the compound containing at least one carbocyclic ring by virtue of the joinder of a pair of R groups.

2. A compound according to Claim 1, which contains not more than 24 carbon atoms.

3. A compound according to Claim 2, where, in the formula,  $R_1$  and  $R_2$  are joined together,  $R_3$  is hydrogen or a methyl group, and  $R_4$  is an alkyl group.

4. A compound according to Claim 2, where, in the formula,  $R_1$  and  $R_2$  are joined together,  $R_3$  is hydrogen and  $R_4$  is an arylalkyl group.

5. A compound according to Claim 2, where, in the formula,  $R_2$  and  $R_4$  are joined together,  $R_1$  is an alkyl group and  $R_3$  is hydrogen or a methyl group.

6. A compound according to Claim 2 where, in the formula,  $R_2$  and  $R_4$  are joined together,  $R_1$  is an aryl group and  $R_3$  is hydrogen.

7. A compound according to Claim 2, where, in the formula,  $R_1$  and  $R_3$  are joined together and  $R_2$  and  $R_4$  are alkyl groups.

8. A compound according to Claim 2, where, in the formula,  $R_1$  and  $R_3$  are joined together,  $R_2$  is an alkyl group, and  $R_4$  is an aryl group.

9. A compound according to Claim 2, where, in the formula,  $R_1$  and  $R_3$  are joined together,  $R_2$  is an arylalkyl group and  $R_4$  is an alkyl group.

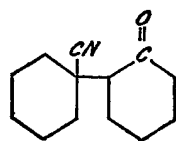
10. A compound according to Claim 2, where, in the formula,  $R_2$  and  $R_4$  are joined together and  $R_1$  and  $R_3$  are alkyl groups.

11. A compound according to Claim 2, where, in the formula,  $R_2$  and  $R_4$  are joined together,  $R_1$  is an alkyl group, and  $R_3$  is an arylalkyl or alkylaryl group.

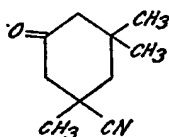
12. A compound according to Claim 2, where, in the formula,  $R_1$  is joined to  $R_2$  and  $R_3$  is joined to  $R_4$ .

13. A compound according to Claim 2, where, in the formula,  $R_1$  is joined to  $R_2$  and  $R_3$  is joined to  $R_4$ .

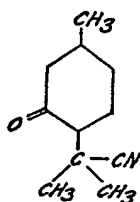
14. The new compound of the formula:



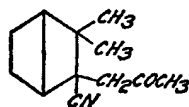
15. The new compound of the formula:



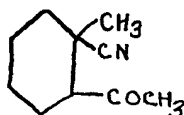
16. The new compound of the formula:



17. The new compound of the formula:



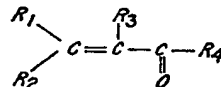
18. The new compound of the formula:



19. The compound 1 - (2 - oxopropyl)cyclohexanecarbonitrile.

20. A method for the preparation of a compound as claimed in Claim 1, which comprises

bringing together, at a temperature in the range from about 125° to 275° C. and in the presence of an alkaline catalyst capable of generating cyanide ions, hydrocyanic acid and  $\alpha,\beta$ -unsaturated ketone of the formula:



in which  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  are as defined in Claim 1, or a  $\beta,\gamma$ -unsaturated tautomer of such ketone, and hydrocyanic acid being brought into contact with the ketone at a rate which is substantially that at which it reacts with the ketone.

21. A method according to Claim 20 carried out by bringing together, at the reaction temperature, preformed mixtures of (a) the alkaline catalyst and the unsaturated ketone reactant or the desired cyano ketone product and (b) hydrocyanic acid and the unsaturated ketone reactant.

22. A method according to Claim 21, wherein the catalyst mixture (a) is initially charged to a reaction vessel and the hydrocyanic mixture (b) is then gradually added thereto.

23. A method according to any one of Claims 20—22, wherein the reaction is carried out at a temperature in the range from 150° to 225° C.

24. A method according to any one of Claims 20—23, wherein the reaction is carried out in the presence of a volatile inert highly polar organic solvent.

25. A method according to any one of Claims 20—24 as applied to the preparation of a compound as claimed in any one of Claims 1—19.

26. A method according to Claim 20, when carried out substantially as described in any of the foregoing Examples.

27. Cyanoketones whenever prepared by a method according to any one of Claims 20—26.

For the Applicants,  
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